not.

The number of adults enrolled was 218, as has been described, and a little under 50 percent have been provided here. The reason for that has been addressed, and we can discuss that, if we would like, in the future or later on.

I can tell you as a reviewer this seems to be a fairly common event, and it is quite distressing in terms of looking at a study that was designed to enroll a number of patients that seems reasonable, and then frequently as in others a substantial proportion less than that are brought to the table for the panel to review. And I would like to encourage the agency and sponsors to live up to their expectations when they present before the panel. It would make it a lot smoother and a lot easier

With regard to the enrolled subjects, demographically a neat proportion, almost 92 percent, were Caucasian. Even though there was a wide distribution at these clinical sites, 11 or 12 sites. The importance of this is the fact that there is some data out there that suggests that geometry of the cornea of various different ethnic groups are different, and the peripheral geometry

of corneas undergoing orthokeratology or CRT by history seems to be important, so the peripheral decentricity values have some role. And so the implication here is that the success or lack of success for groups other than Caucasians may not be the same as for Caucasians, and the panel may want to address this issue in labeling.

Including the partial corrections in this PMA was actually somewhat troublesome for a while. Now, I understand the role of this, to incorporate a larger number of individuals from the safety perspective, but as a reviewer I can say that this was a little bit disconcerting, dealing with individuals who are enrolled under a monovision environment and then being included in visual acuity information.

The discontinuation rate of these subjects was impressive, but not unlike other studies that have been done with regard to orthokeratology over the past. However, I think it's important that doctors and their patients know what the discontinuation rate was, and I would request that this be included in the labeling.

Clearly the number of patients who are in the minor age group was quite insufficient for any

evaluation, and I would encourage that we consider at this time labeling that indicates that we do not know what the safety and efficacy is in children. I do not specifically recommend that we exclude children, but that we just don't have data on that information presented.

Also, there were a number of conditions, medical conditions, that were excluded from individuals in the enrollment criteria, that are not specifically excluded in the labeling, and I would encourage that we consider using that same criteria or at least address in the labeling those conditions that were excluded, where we don't know what the safety and efficacy is in that population of individuals.

The accountability for this study was excellent, and the sponsor and the investigators are to be congratulated for adhering to that schedule. The efficacy of CRT in achieving emmetropia within a half diopter, 1 diopter, and 2 diopters, the last of which I'll ignore, since I think within the cohort that we're dealing with of plano to minus 6, plus or minus 2 diopters is not a very meaningful number.

About half the patients, as previously

demonstrated by the sponsor, were within a half a diopter of their intended or within plus or minus a half a diopter at the various different periods that were measured, one, two, three, six, and nine months, and about 90 percent were within plus or minus 1.

Though it hasn't been mentioned yet, there is a small trend towards continued improvement as time goes on, somewhere close to about a quarter diopter per year. Now, how long that is going to persist, I don't know, but since the majority of the patients that did not achieve 20/20 were in the undercorrected group, I'm not worried by this. In fact, I'm somewhat encouraged that there may be a little bit of increased treatment as time goes along.

Clearly for those that discontinued treatment, that band of individuals were more likely to be outside the plus or minus half and 1.

The plot before you or the graph before you is a post-treatment uncorrected visual acuity for 20/20 through 20/80 and worse, as a function of their pre-treatment manifest refraction spherical equivalent. This is for all efficacy eyes, which is the 168 eyes mentioned on the table at the

bottom of the graph.

And what is clearly evident is that the effect of this in all eyes that are analyzable drops off, in terms of best treated visual acuity, relatively remarkably as you move up the refractive error schedule. In fact, after you go over 2 diopters in myopic refractive error, that number drops to actually less than 50 percent.

At the same time, in the 20/30, 20/40 range, which is an number that's commonly used, for example, in refractive surgery arenas, those numbers are actually still quite impressive. If we look at those individuals who are in the targeted emmetropia group, which is a slightly smaller subset, the numbers look approximately the same but a little bit better.

In short, if one chooses 20/20 as the desired outcome, this procedure does not appear to be very effective under the paradigm employed by the sponsor. However, if you use a looser criteria such as 20/40, it appears to be quite effective.

There was relatively little astigmatism in the pretreatment group, and of the 168 efficacy qualified eyes at six months, about 66 of these patients had increases in astigmatism, 43 had a

decrease, and 26 had no change, and there were only seven that had an increase greater than 1 diopter. It would be helpful to see those that discontinued treatment, the 40 percent or so, what their astigmatism characteristics were like, and I don't think we have seen that information.

However, the amount of astigmatism that is either increased or decreased, for that matter, appears to be actually quite small and I think is a minor issue, and those changes appear to be less for both increases and decreases at nine months as compared to six months. The bottom line here is that this procedure does not appear to do much for astigmatism in a negative way or in a positive way.

As has been mentioned, a number of lenses were used under what in the initial protocol was described as a retreatment lens, of which about 60 of the 70 were really retreatment issues and the other ones were replacements, and at this juncture we have not seen data with regard to the effect of that, and I'm not sure what to do about that, quite frankly.

With regard to stability of the treatment effect, from three to six months, 76 percent of the eyes treated demonstrated less than about a half

diopter difference than their subsequent post-treatment refractive error. Eighty percent demonstrated this at six to nine months. For the differences of less than or equal to a diopter, those numbers increased to 95 percent and 91 percent at six and nine months, respectively. The confidence interval crossed zero at all times but, as I mentioned before, there does appear to be this slight trend towards improvement at about a rate of a quarter of a diopter a year, "improvement" meaning decrease in myopia or hyperopic shift.

This plot demonstrates the treatment effect in the percent of patients 20/40 or better--or in number of eyes, I should say--and this pertains to what the visual acuity of the refractive error is, or by a function of refractive error. So, for example, for patients less than or equal to minus 1 at eight hours, four of those subjects are qualified for this, 100 percent of them at 20/40 or better, and also at 24 hours.

The sponsor has carried this out to 72 hours, as well, and there's two trends that are evident. One is that with time the effect decreases, which is not unreasonable to expect, and two is that those with high refractive errors tend

to degrade in terms of their effect more rapidly.

What I think is a glaring omission in this PMA, and though the FDA guidance document addresses this, it's in a way that I think may justify some reconsideration, is the mean time to recovery from treatment. The sponsor went out to the level of three days but no further than that, and in those patients with low refractive errors, these patients still demonstrated 20/40 or better visual acuity during that period.

I think it might be very valuable for this information to be available to the patients and their doctors, so they can advise patients as to the course of this if these patients discontinue treatment. And it's clear that a substantial number of patients who are going to undergo CRT are going to leave treatment. In the study alone it was 40 percent or so.

This appears to be a safe procedure, and that's probably the most important thing with regard to this PMA. At nine months, 68 percent had no change in best corrected visual acuity, 13 percent will become poster children because they had one line of increase in best corrected visual acuity, and 1.6 percent had more than two, and

we'll see them on TV advertising this very shortly.

A similar number of these individuals also demonstrated decreases in visual acuity, and as the sponsor demonstrated, these appear to be transient changes.

For those of you who prefer charts--Dr. Grimmett--this data is described on the plot that you see here, and the vast majority of patients actually demonstrated no change. An equal number show increases versus decreases.

Appendix No. 3, Tab D, pages 110 through 112, defines to what level and what extent there are losses of two lines or more, by material, and as can be demonstrated, there really is minimal difference between the two, though symptomatically there appears to be more trouble with individuals using the low Dk material, which is not surprising.

The question has been raised a number of times thus far, why would an individual want to use the lower Dk material? And I raised the same question, and I have not heard a satisfactory answer. At the same time, I recognize that both these materials have been approved for extended wear, and I'll leave it at that.

A number of slit lamp findings are

relatively mild, and those with greater than Grade 2 slit lamp findings were quite rare, suggesting this is indeed a safe procedure.

Finally, in conclusion, orthokeratology has been around a long time. It has been around as long as I have been in practice, and I'm pleased to see that this proposal is helping bring the whole area into the region of science, as I said, relative to cultish thinking.

With regard to this PMA, the overnight use of lenses to change the shape of the cornea in a safe manner is really the real question before this panel, and I think this PMA has demonstrated that CRT is both safe and effective for the indications that the sponsor has requested. Thank you.

DR. WEISS: Thank you, Dr. McMahon. We're going to proceed with the panel review from Dr. Timothy Edrington.

DR. EDRINGTON: This will be brief. The sponsor designed the study and methodology, including the sample size and study duration, I think appropriately to determine the primary safety and efficacy endpoints. Dr. McMahon and others have gone over the results in great detail, and so I'm not going to repeat the results. I have

nothing to add in that regard.

I guess the bottom line in one respect is patient happiness and patient satisfaction, and it's reported here that more than 90 percent of the patients had good, very good, or excellent as their interpretation or their evaluation of the treatment.

So basically what I would like to discuss is sort of recommendations, and one recommendation would be that there be sufficient training and perhaps certification for fitters. I have been exposed a little bit to the fitting philosophies involved, and it is definitely unique relative to what we traditionally think of in terms of fitting rigid contact lenses, and even very experienced fitters will need some hand-holdings and guidance and definitely some training, so I think that is an absolute must for this to be successful on the public.

Also, as I read the package inserts, I got confused from time to time in terms of what was written for the practitioner and what was written for the patient. I think those books or information booklets for both the practitioner and the patient need to be written differently. I

think they need to be provided with a lot of information that was covered today, and I think the patient does as well. The patient needs things such as the table looking at the post-treatment visual acuities, to find out with their refractive error what their expectations should be.

And again on these books, there should be informed consent document sort of detailing the treatment, the limitations, the outcome expectations, and the risk, including symptoms and signs. And also the patient needs to know the length of time until they can expect the treatment to be adequate or stable. You report in findings that there is stability from one to nine months, but it really doesn't tell us at what point the effect is sort of to its end point.

And the patients really need to know the fact that they are going to need to wear the lenses on a nightly basis, at least for the patients with 2 diopters or more of myopia. I think patients these days are looking for very quick solutions to things. They know a lot about Lasix, and with that in mind, they're maybe thinking that this is going to be a one-night wear and they're through with lens wear. I think this has to be very, very

clearly laid out to the patient.

Also, I think they need to know that there is a large percentage of discontinuations, not only in your data but also in Polse's data, a very high percentage of discontinuations. So they need to know that on the front end, that not everybody is satisfied or comfortable with this therapy.

But I would recommend premarket approval for the CRT for overnight wear for myopia at the 6 diopters, but at this point in time, until further follow-up data are reported for the adolescent cohort, I would suggest approval just for ages 18 and over. Thank you.

PANEL DISCUSSION OF P870024\S043

DR. WEISS: Thank you, Dr. Edrington.

We will then proceed to the panel discussion of this PMA, and I'm going to suggest we go through the FDA questions for the panel discussion question-by-question. Would you be able to put those up, as well? Thank you.

The first question is going to be, "Do the data reported for the two different generic lens materials evaluated during the study raise any questions of safety and effectiveness?" We can start the discussion while they're getting that up

on the screen. Maybe one of the--Dr. Edrington, can you guide us on that?

DR. EDRINGTON: Tim Edrington. The data that we reviewed sort of indicated that they were substantially equal, or equivalent, maybe that. And again, I'm not sure we were really provided enough data to make that call ourselves. The data wasn't provided to us today, but the company makes me feel okay about both lens materials being approved.

But there seems to be no compelling reason to me, as a clinician, not to use the higher Dk material. And that's I think what I was sort of fishing for when I was asking are there manufacturing or fabrication issues. Are there some issues as to why the other material should be utilized? I do understand there are doctors that still prefer PMMA lenses out there, but I'm not sure that is how we make our recommendation. I would lean toward, I would personally tend to use the higher Dk, unless my clinical experience after I used it told me to try the other. But again, I saw no compelling evidence one way or the other.

DR. WEISS: Dr. McMahon?

DR. McMAHON: I'm a little torn by that

issue, and we're somewhat constrained by the fact that both these materials are currently approved for extended wear. And I'm wondering, if we approve just one of the materials, whether that's an undue burden or hardship on the manufacturer that's not appropriate. The data doesn't suggest at this point that--but it's not a lot of data--that there is any increased risk, other than maybe a high altitudes. I think I would be most comfortable in specifying what the transmissibility values are and then let the practice of medicine and optometry go from there.

DR. WEISS: Any other comments on this question? Dr. Van Meter?

DR. VAN METER: Van Meter. I think it would be possible to say in labeling that if it is approvable, even to let them use both materials, and to say that evidence of corneal edema exists at high altitude which actually occurs with both lenses, and somehow warn this as an issue that both patients and clinicians can be aware of. Then I think we're probably within reason to approve both materials.

DR. WEISS: If all are agreed, we can go on to Question No. 2: "Do the data reported for

the two reverse geometry lens designs evaluated during the study raise any questions of safety and effectiveness?" Dr. Harris?

DR. HARRIS: Michael Harris. Well, the question is an appropriate one, and one that was raised earlier, and the issue is, are we willing to accept the data on the Quadra design from the other studies and say that it's going to basically give us the same safety and efficacy as what's presented today and in the materials we received earlier on the CRT design.

And again, as with the issue of the two different materials, I am torn. I would have really appreciated seeing some data on the Quadra design on the exact same study design to be able to make this determination. Without that, it's somewhat of a leap of faith to say that we can equate the safety and efficacy data from a totally different type of wear to what's going to happen with this.

I certainly have no problem with the CRT design. The sponsor has provided sufficient data to indicate that it is safe and effective for the intended uses, but I still question whether or not we can make that leap of faith to approve the

Quadra design for the same uses.

DR. VAN METER: Any other thoughts on this issue? Dr. Bradley?

DR. BRADLEY: I think I've made these comments at previous panel meetings regarding corrective surgery. It's unique for me to be able to make these comments now about a non-surgical procedure.

Just looking at the data tables, I mentioned looking at, there's a series of tables in the original submission, page 83 through 87, which breaks out the visual acuity AL post-removal for the different refractive error levels. And once we get beyond a starting refractive error of one diopter, and we look at the 20/40 or better data at eight hours post-removal, we see for the 1 to 2 diopters we're at 90 percent, for the 2 to 3 diopters we're at 85 percent, for the 3 to 4 at 87 percent, and for the greater than 4 diopters we are at 76 percent.

And they always look pretty impressive, particularly when you're around 90 percent achieving 20/40 uncorrected visual acuity, and that's really the argument that we've heard many times from the refractive surgeons. But in the end

I just find that rather worrying, because 20/40 acuity is really not very good, and I think in the past having 10 percent to 15 percent of your patients who cannot achieve 20/40 has been deemed marginally acceptable. And I think it's worth considering that 10 to 15 percent of these patients may not be able to drive safely because they do not have 20/40 acuity, and I just find that a potential safety issue, although it was generally considered as an effectivity issue.

I'm also worried a little bit about the recovery cycle, particularly with regard to night driving. And of course the patient is taking the lens out early in the morning and may be doing their night driving at more than eight hours post lens removal, and one wonders about the level of acuity and general visual quality achievable at this particular time, which arguably might be the most critical time of the day, in the sense that the pupils will be dilated and any refractive error manifest at night would have its greatest impact under those conditions. So I'm a bit concerned about that.

And although the consensus this morning seems to be that the device is effective, I think

the data are not that impressive, in the sense that 10 to 15 percent of the people are not achieving uncorrected visual acuity of 20/40. As the sponsor has alluded to, this may be rather an under-estimation of what the product can achieve in the real world clinical environment, because the final effect may be tweaked by modifying the lens or refitting. But in the actual data submitted, I still find 10 to 15 percent of the patients not achieving 20/40.

DR. WEISS: I think that's something that can also be addressed in labeling, in terms of informing the patients that for the higher myopic errors, their expectations should be much lower.

I would like to get back to the issue of the reverse geometry lens design, in terms of perhaps coming to some consensus or more discussion at this juncture as to whether the Quadra is something that people feel comfortable with or do not feel comfortable with in terms of the lack of data. Do any of the primary panel reviewers have opinions on that? Dr. McMahon?

DR. McMAHON: My initial view was "no way," because there's no data, but as time goes along I guess I'm mollifying my view to some

degree, in that the designs are really not that dramatically different. They both employ essentially a reverse geometry design. It's primarily the intermediate or the transition zone, sometimes referred to as a "landing zone," that is constructed differently, and then the peripheral curves are curved in one and straight in the other. The likelihood that these will be meaningfully different with regard to safety is probably very small.

With regard to effectiveness, I have no idea. Probably, if I had to guess, it would be fairly equivalent. The cornea is pretty robust and responds in certain ways, and I think that they're not too different. So my inclination is actually to approve it at this time.

DR. WEISS: Dr. Rosenthal, did you have a comment?

DR. ROSENTHAL: I just want to comment, this is a Class III device, for which clinical data should be provided to support reasonable assurance of safety and efficacy. As with all devices there are modifications to devices which occur without clinical data, based upon the proposal set forward by the company, and the panel really has to decide,

not probably but based upon a reasonable argument, scientific argument, that the design of this lens will perform exactly as the lenses that have clinical data.

DR. WEISS: Dr. McMahon?

DR. McMAHON: Since this panel wasn't presented with any data, including the daily wear approval data, if we adhere to that criteria, then I'd have to change my opinion.

DR. ROSENTHAL: Rosenthal. Well, you know, there is daily wear data that the company has submitted. You may not have seen it, but--

DR. McMAHON: We're being asked to rule on it.

DR. ROSENTHAL: Well, possibly the company and the agency should have provided you with that data, but you could make one of several recommendations regarding that, based upon your scientific judgment as to whether or not it, you know, would be applicable or not.

DR. WEISS: Dr. Saviola?

DR. SAVIOLA: To further elaborate on the clarification from Dr. Rosenthal, the data regarding the daily wear outcomes is provided in the labeling for the RG design in both materials,

so that part of the labeling section of the panel pack does have the outcome data from there.

From the standpoint of--one of the reasons why we have it here today and asking this particular question, is to gain from you what your clinical impression is; for example, the comments you just made, Dr. McMahon, regarding what your expectations might be, because in actuality none of us have any data on the RG in the overnight wear scenario.

However, you are our panel of clinical advisory experts, and so those of you who have experience and knowledge of these different designs to weigh in and say, well, yes, the difference between the sigmoid aspect in a three-zone RG design versus a four-zone, what are your expectations on that? We certainly have opinions internally but we're not going to share those with you at this point. We're looking here at what you have to say and then go from there on your recommendation.

DR. WEISS: Dr. Edrington, and then Dr. Smith.

DR. EDRINGTON: I guess I'll share my opinion.

DR. WEISS: I want to know if you're mollified.

[Laughter.]

DR. EDRINGTON: I would, in terms of safety, assuming the lens profiles are the same--and again, I don't know what the thickness profile of the Quadra design is--assuming it's similar, and assuming its plano power, I would think the safety issues would be similar. I don't see there would be a big difference there.

In terms of efficacy, it would have to be my guess that one of the reasons that they might want the Quadra design out there is either backup in terms of the CRT doesn't work, I don't know if there's a price point difference, and I don't know if you have to be trained. Perhaps you don't have to be trained and certified for the Quadra.

So that might be my impressions as to why Paragon might be asking for this, but again from safety I have no additional concerns.

DR. WEISS: Dr. Smith?

DR. SMITH: Janine Smith. Two comments. One is to Ralph. Is there any precedent for approval of a material like this without clear data presented in the PMA, in any other contact lens or

other ophthalmic device?

DR. ROSENTHAL: Rosenthal. Just generally, you know, devices are always, they are always--and I would like Jim to comment on the exact question that you have--but as I said before, devices are always undergoing evolution, and based on scientific knowledge and based on experience, based on clinical knowledge and based on appropriate scientific argument, you do not necessarily have to provide clinical data for changes in devices. You know, in the area of pacemakers, they sometimes change before they even get out on the market, before the studied pacemaker.

So we need the panel's recommendation based upon their scientific knowledge, based upon a scientific justification from the--to confirm a scientific request from the company, a request based on scientific knowledge and clinical experience.

DR. WEISS: Dr. Saviola?

DR. SAVIOLA: Dr. Smith, your specific question, in the history of contact lens regulation back early on for rigid lenses, we did see clinical data for a variety of different alternative

designs. Over the course of time we did modify that, and since 1988-89 for rigid lens alternate designs we basically look at the confirmatory aspects of the design as in any spherical bifocal type, multifocal correction. There are many cases where you approved a variety of alternative designs in a particular material without having clinical data, based on the concept that the material has already been approved for, say, overnight use, and the profiles in terms of permeability and transmissibility are consistent within the currently approved range.

I'd just like to clarify one of Dr. Edrington's comments. The Quadra RG, as the folks at Paragon, Dr. Meyers had said earlier, our understanding at the Review Branch is that the Quadra RG is going to be "licensed out" to the finishing labs, whereas the CRT, the sigmoid geometry which has a little bit higher level of control, is going to be maintained centrally within Paragon's manufacturing only. So that's one of the differences between the two, and I think primarily that's why they are split out like that.

DR. WEISS: I would just ask one question: Have there been any studies done to date taking an

orthokeratology lens which is used for daily wear and comparing it to being used for overnight wear, as far as does it have the same effect?

DR. SAVIOLA: I am not--well, there have been a couple publications of folks at OSU who have used some of the daily wear designs and published, I think, two papers on a small group for a limited period of time, on overnight effect. The actual fact is that currently in clinical practice, that folks are using orthokeratology, and I don't have the exact number, but to a large degree are using it off-label for overnight wear, even though it's only cleared for daily wear use.

DR. McMAHON: A clarification.

DR. WEISS: Dr. McMahon?

DR. McMAHON: For the Quadra design which is now approved for daily wear, which implies power in the lens, I don't recall, does Paragon intend to move this to the plano design for the overnight wear or to include power? Because that changes the transmissibility issues.

DR. SAVIOLA: Right. I'd have to let them answer that question.

DR. McMAHON: Plano?

DR. MEYERS: Yes, plano, always plano, is

the goal.

DR. McMAHON: Thank you.

DR. WEISS: Dr. Bradley, did you still have a question?

DR. BRADLEY: Yes. As somebody outside of this field being asked to make this judgment, I just have to rely on our colleagues here who are very experienced with contact lenses. I just wanted to clarify, perhaps in my own mind, the judgment we're being asked to make here.

The issue is not should we approve a lens for which we have no data. I don't think that's the question here. If that was the question, I think we'd be in a bit of trouble because I think as Dr. Edrington has suggested, probably safety issues are not troublesome here but efficacy certainly is.

I think as the literature shows, and I think as Dr. Bullimore presented, there are other lens geometries out there that have certainly proven themselves not to be able to produce that level of refractive change that the CRT has produced, so there would be no basis upon which to argue general efficacy for all ortho-k type lens designs. So I don't think that's what we're being

asked to do.

I think we're being asked to essentially extend what is known about the Quadra lens from daily wear to nighttime wear, and I think if that is the extension without data that we're being asked for, maybe the primary issue there is one of safety. But perhaps the contact lens--

DR. WEISS: Dr. Harris?

DR. HARRIS: Michael Harris. I understand what you're saying, Arthur, and agree to some extent, but we're being asked to approve this lens for a different use. It's a different indication, and I can't make that leap of faith that the effectiveness of this lens worn eight hours overnight and what that's going to do to the cornea, is the same as where this lens is worn in a more traditional daily ortho-k fashion and what happens.

We're being asked to accept the fact that the patient's likely outcome as far as visual acuity and refractive error is going to be essentially the same as what the data supported for the CRT design, and since this is a different indication and a different use of the Quadra material, I'm really hard-pressed to use the daily

wear data to support an overnight indication.

DR. WEISS: Dr. Bradley?

DR. BRADLEY: So just a follow-up, and I agree with what Mike is saying. The implication of what you're saying, Mike, I think, is that any new geometry must undergo a full-blown FDA clinical trial in order to be approved.

DR. HARRIS: Not necessarily.

DR. BRADLEY: Is that the implication?

DR. HARRIS: No, not necessarily. The agency has all kinds of ways for a sponsor to come back with different designs and provide data. If I remember from the history on this panel, there have been approvals for a particular design or a particular material and rather than come back to panel, the sponsor has been able to go to the agency, provide the supporting data to show that this new design or this new material effectively meets the criteria that were set when the original approval was made, and therefore not have to go through a full panel evaluation.

DR. BRADLEY: Just a clarification. I didn't say they would have to come back to the panel, but they would have to perform another clinical trial. And if that is the implication,

the follow-up question becomes, how much of a change in geometry requires a new clinical trial? For example, if they were to change their CRT base curvature or something, is that a sufficient change in geometry? You know, where do we draw the line for practical purposes?

DR. HARRIS: That is obviously a question for the agency to determine, and not for us as panel members. But as a reviewer, I don't mean to skirt the issue, but the agency would have to decide whether or not a certain change in design and materials required a review or could get by with something less than a full review.

As a clinician reviewer, asked to evaluate a particular design in a particular material, I am hard pressed to indicate that (a) that a design and material are safe and effective when I see no data on the safety or effectiveness of that design for the use that is being asked for, and that is the case that we have here with the Quadra design.

DR. ROSENTHAL: May I just clarify it? A sponsor can make arguments based on clinical data, nonclinical data, theoretical data, a theoretical analysis, and then the agency has to -- in supplements to their existing application -- and

the agency has to then make that decision.

We are currently asking the panel to make this decision based upon the information they have available to them and the information which the sponsor has provided to them.

DR. WEISS: Dr. Bradley.

DR. BRADLEY: Maybe the sponsor could answer this. It looks like we are going to have to make that decision today, and so I would like to hear somebody convince me that the Quadra is approvable.

DR. ROSENTHAL: I don't think that is appropriate because it would be discussing issues that have not been presented in the PMA. If the panel feels that they cannot make the determination today, they can suggest a way in which a determination could be made.

DR. WEISS: Dr. Smith.

DR. SMITH: I just have one question as I am trying to think about this, like the rest of you on this panel. If we were presented with a daily soft contact lens that had already been approved, and a new indication for extended wear for the same lens was being sought, I don't think that any of us would say that we could make any determination

without data.

DR. WEISS: I wouldn't think, though, Dr. Smith, that this is the same situation because this is not a new indication. It was used for orthokeratology. The whole question is if you close the eyelid all night, are you going to have a problem. It is going to be used for the same indication, the same amount of time.

DR. SMITH: Extended wear would be the same indication for correction of vision

DR. WEISS: For a longer period of time. This is still going to be eight hours, but it is eight hours with the eyelid closed versus eight hours with the eyelid open, and I don't think anyone in this room knows the answer.

DR. SMITH: Well, I think that the point is that the eye being closed is different than the eye being open, and I think we do need that.

DR. WEISS: But I think Dr. Bradley's comment is well taken, at what point do you call it a variable, at what point is it a variable versus just acceptable.

Dr. McMahon.

DR. McMAHON: In clarification, it is not as simple as saying a daily wear approved design

for extended wear because we are talking about materials that are already approved for extended wear, which the nature of the material is the most important issue with regard to extended wear in any kind of lens, soft or hard, that we have had to deal with today.

So, this is a little bit more unique and that taking an indication, for one thing, an approval for material for another, and put them together on a clinical leap of faith. In sort of hanging on Dr. Rosenthal's every word, he said two things, and one I can deal with and the other I can't.

The first one he says based upon my scientific evidence, and the other one was about my clinical judgment. I have no scientific evidence. The answer for that side of the equation would have to be no. Based upon the clinical judgment, based upon my experience, which includes the leap of faith, and so forth, I suspect that there is not much difference, and I would be comfortable with it.

DR. WEISS: So, your mollification level now is the same.

DR. VAN METER: Would it be possible to

approve the lens with a condition, the labeling would specify that data for effectiveness for the Quadra lens has not been determined?

DR. WEISS: I believe that we can say that.

Dr. Rosenthal?

DR. ROSENTHAL: You can recommend, you are advisory to the agency, you may recommend as you feel it appropriate to recommend based upon your judgment.

DR. VAN METER: I agree. My clinical judgment is that the lens is probably okay, but we haven't seen data, and I think if we just say that the data is indeterminate.

DR. ROSENTHAL: Dr. Van Meter, if that is what you wish to recommend, I would appreciate you recommending it.

DR. McMAHON: I would actually support that. I think that is a way of dealing with it.

DR. WEISS: Thank you, Dr. Van Meter. On that note, we will move on. Question No. 3.

DR. HARRIS: Excuse me, Madam Chair.

DR. WEISS: Yes, Dr. Harris.

DR. HARRIS: Have we reached a consensus on this?

DR. WEISS: Let us see the consensus. Dr. Harris, have you changed your opinion on the basis of what has just been said, or what would you feel comfortable with at this point? Maybe we can go around and get some idea of what the panel members feel at this point.

DR. HARRIS: I understand the argument being made, but I cannot agree with it.

DR. WEISS: So, you would choose not to have the Quadra as part of this PMA.

DR. HARRIS: Yes, I would obviously give the sponsor the option of coming back with additional data to support that at a later time, not necessarily having to go through the full-blown FDA review, to get approval for that other design.

DR. ROSENTHAL: Excuse me, Dr. Harris. They have to go through a full-blown FDA review. They don't have to go through a full-blown panel review.

DR. HARRIS: I apologize. That is what I meant. Thanks.

DR. WEISS: A full-blown will be part of it unfortunately. Full-blown. FB.

So, Dr. Harris, you would not like to include the Quadra. Dr. Casey?

DR. CASEY: I would agree with Dr. Van Meter's recommendation.

DR. WEISS: Dr. Edrington?

DR. EDRINGTON: Since I feel somewhat safe with the safety portion of it, it is the efficacy that remains the unknown, I would agree with Dr. Van Meter in terms of approving it, but the labeling indicate to both practitioner and patient very clearly that there is no data to support that at this time.

DR. WEISS: By the way, this is totally informal, so if you have any additions or alterations, please voice them now, so that when we get to the final vote, we can have a clear idea where everyone is at.

Dr. McMahon?

DR. McMAHON: Addressing the absence of the data for safety and efficacy for Quadra and the labeling, I think would be sufficient.

DR. WEISS: Dr. Matoba?

DR. MATOBA: I agree with Dr. Van Meter.

DR. WEISS: Dr. Bradley?

DR. BRADLEY: I would like to see the FDA require the sponsor to present, not to us, but to the FDA, some data in which they would use to argue

effectiveness and safety for this lens. We have not seen that data, and I just feel uncomfortable approving such a lens, but I could foresee that the sponsor has those data.

For example, they can argue effectiveness based upon their daily wear, and they can argue safety based upon the known properties of the material being used. So, I don't see any problems with the sponsor producing that argument, but we have not seen the data, and I don't think we can really make any judgment.

DR. WEISS: I see sponsor shaking their head in the affirmative. Do you have this data? I mean not here, obviously, but would we be in a position to say this is approved pending the submission of data to the FDA?

DR. ROSENTHAL: The panel may make recommendations as they see appropriate.

DR. WEISS: Do you have this data? We are not going to ask you to present this data, but is it available if we ask for it at a future time?

DR. MEYERS: We certainly have the daily wear data and have already submitted it to FDA, and by the way, we are only asking for an indication for efficacy based on that daily wear data.

DR. WEISS: What I am asking specifically, do you have the data for the indication that you are asking for approval for, namely, the use of the Quadra lens as an overnight orthokeratology lens?

DR. MEYERS: Well, that would depend on how many patient -- I can't answer that question in terms of how many patients would be required to submit this data.

DR. WEISS: So, it is not clear whether that data is available.

DR. BRADLEY: Madam Chair, just a clarification. I wasn't suggesting they produce those data, but any data from which they can base an argument of either equivalence or effectiveness or safety.

DR. WEISS: Dr. Bullimore.

DR. BULLIMORE: Just to clarify the sponsor's position, we are asking for approval for this design based on the safety profile for the other design as demonstrated in the urbanized study and based on the efficacy of the daily wear approval.

As I stated before, traditionally, even though this is considered by the FDA to be a Class III device, approval for contact lenses has been

based primarily on the safety of the material and the indication. Those two things are the same.

Certainly, we would consider the differences between the two designs to be significant enough, such that the two designs do coexist, but really, as some of the eminent panel suggested, that there to be subtle differences in one area of the lens, and in terms of its safety profile, were very comfortable that it would be equivalent.

DR. WEISS: There wouldn't be any data for anyone to review, just rather than making a leap of faith or our own conclusions?

DR. BULLIMORE: Other than to direct the panel that Dr. Rah's data presented in the public session, and we have not had a chance to review that data, but that was, in fact, used in the design analogous to the Quadra design.

DR. WEISS: I would probably like to close off the comments from the sponsor unless there is anything additional new to add at this point.

DR. LEGERTON: This is an answer to the same question. As Dr. Bullimore indicated, Dr. Rah did present two designs in the public session. One was the Fargo 6, which is an example of what the

Quadra RG approval would be used for. She had 25 subjects in the Fargo 6, she had 30 subject in CRT.

Also, there is published literature, refereed literature, the Nichols' article of the 60 nights of continuous wear, overnight wear, was with a non-CRT, but it was in the Paragon HDS material.

So, you do have published literature, and you did have a presentation in a public session. It does give you examples of what were equivalent outcome to what we presented in effectiveness. However, again, we aren't requesting that level of effectiveness. We are requesting a labeling up to 3 diopters of myopia with 1 1/2 diopters of astigmatism, and the outcome percentages that were achieved in daily wear, so we are taking that compromise, we will say, reduction in the labeling.

DR. WEISS: Just for the panel reviewers, the lenses that were mentioned that were fairly equivalent, the variable, how does that compare to the Quadra versus the CRT, and in terms of does that help you at all saying the Quadra is going to act the same as the CRT in nighttime wear, or these are all different shaped, and so you can't really form any equivalency?

DR. McMAHON: They are not equivalent, but

they are similar.

DR. WEISS: Similar enough that --

DR. McMAHON: I think so.

DR. WEISS: Fine. We will go on.

Dr. Grimmett?

DR. GRIMMETT: I think the people in attendance would know my opinion for liking to review the data. I think the sponsors just indicated that literature does exist regarding the indication they are requesting, so that being the fact, I would agree with Dr. Bradley's sentiments, that it is not unreasonable to have the FDA perform the usual due diligence on data that the sponsor presents, arguing for the change in indication.

I have not personally reviewed that data in sufficient detail to make the decision at this table, but I think it is not unreasonable to go along with Dr. Bradley's request.

DR. WEISS: Dr. Coleman.

DR. COLEMAN: Yes, I agree with Dr. Grimmett and Bradley.

DR. WEISS: Dr. Ho.

DR. HO: I am comfortable with an FDA due diligence review of information and the labeling disclaimer.

DR. WEISS: I just want to clarify. So, you would be comfortable with approval with the labeling information saying that we don't have data on this?

DR. HO: Correct.

DR. WEISS: Dr. Van Meter, who raised this interesting point, we know your opinion I think.

Dr. Smith.

DR. SMITH: I agree with Dr. Bradley and Dr. Grimmett.

DR. VAN METER: So, is the question that we definitely are going to put a labeling disclaimer, and plus or minus FDA due diligence?

DR. WEISS: Well, I think the question is whether the panel -- and it is split at this point -- feels that we have enough information for the Quadra to be approved with the stipulation that you stated, having the information in the labeling that we don't have the data, versus half of the panel who feels that it cannot be approved because we don't have the data. So, it is split at this point.

Did we mishear you, Alice? You changed your mind? Which side are you on? You have moved to the Bradley side. Well, then, it is no longer

split. In that case, I won't have to vote, which is nice.

We will move on to Question 3. Is the length of follow-up sufficient to demonstrate the stability of the intended myopic reduction with the prescribed maintenance regimen?

Dr. Edrington.

DR. EDRINGTON: In terms of the length of follow-up, looking at follow-up in terms of months, and such, it appears the data looks fairly stable after one month, all the way out to nine months. I guess the longer term follow-up would be nice to see if there are long-term complications to the procedure, but I feel fairly comfortable with the amount of follow-up that was provided.

Actually, Dr. Bradley, I thought, relative to a couple points ago, brought up an interesting point, which is the stability during the day, and we were provided with data for eight hours and 24 hours.

Dr. Bradley brings up some interesting nighttime driving issues, which might be 12 or 16 hours out, or 20 hours out, and that data is not provided to us. I assume that Paragon does have that data, and I think that is something that needs

to be strongly put in the patient education and in all the labeling for both the practitioner and patient, because that does raise a little area of concern.

DR. WEISS: If there is no other discussion on that, we will go on to Question No. 4.

What are the panel's recommendations for the proposed product labeling, warnings, precautions, terminology to describe the procedure?

Dr. McMahon.

DR. McMAHON: At the end of my handout, actually, I have a summary of labeling issues that I would like the panel to consider.

Glenda?

MS. SUCH: There is a couple of things in the labeling that concern me. One is that it appears as though in the first 20, 40, 60 pages of this document I have here, in the labeling, it is writing to two audiences. It is writing both to the physician, and it is writing to the patient at the same time, and I would like to see that clearly pulled apart, either that or recognizing, pull it out in some bulleting or something that would make it more clear.

I find myself reading through and suddenly realizing, okay, I am not reading as someone else, and literally, it is addressed to the person themselves as you will do this or you will do that, or this is suggested for you.

The other pieces, with respect to in the Patient Information Section of the labeling, that because this is being read by your typical patient, then, I am concerned that when it talks about the temporary reduction of the myopia, that you are looking at people again, as has been said in the panel, that we are talking about eight hours, and then there being a very significant drop-off rate between the eight-hour mark and the 24-hour mark for people that are above 2 diopters.

I am concerned that the word "temporary," people understand that, that that means halfway through their day, literally, halfway through their workday or whatever, that they are now going to be in the need of going back to using their lenses or going back to using glasses, to the point where a lot of different types of duties that would be in their way, whether it be driving or whether it be crossing streets or reading signs, or anything, would be greatly compromised, so I think that needs

to be very clear that we are talking about that after eight hours, half a waking day, half of what you need to do in that day, if you were in that greater than 2 diopter need, that you are definitely going to have to change.

So, this is the temporary wording. The word "temporary," I think while I don't want to have it so that the sponsor feels as though they have to limit this so much that they can't market the device, so much as saying okay, well, our device is good for only half your day, but rather looking at a way to be able to prevent that, not so far in the cautionary.

You don't want yourself set up for people to come back and criticize yourselves and say that we are promoting something that really has a fall-off rate.

DR. WEISS: Dr. Matoba, did you have a comment?

DR. MATOBA: [Off mike.] I want to add that I think we should state that nearly 20 to 25 percent of people who are fitted may have discontinued it because of inadequate vision.

Also, something about the fluctuation in vision. That is, these patients who have

uncorrected visual acuity decreasing six months out, nine months out, I wanted to have a little bit more information about the exact nature of that problem, because it is one thing if they are 20/30 and then one day they are correctable to 20/20, and the next day they are not, but they are walking around with 20/30, and they don't perceive a difference, and it is another if they are walking around with 20/20 and suddenly they are 20/30 or 20/40, and they can't be corrected.

I don't want to be on a plane and have my pilot have a bad hair day. I would like to know exactly what happens when they have those problems that occur, and the labeling should reflect whatever those circumstances would be.

DR. WEISS: Dr. Harris.

DR. HARRIS: Dr. McMahon, on the last page of his handout material, has a summary of some labeling issues. Is it appropriate for us to let him lead the discussion and then comment on it?

DR. WEISS: Very good. I mean it would be nice to have some consensus on the various labeling issues at this point, if we can.

Did you want to go through each of those, Dr. McMahon?

DR. McMAHON: I would be happy to.

Item No. 1 is include a table of DK/T values for the range. I assume that a len power is involved, so that is not relevant at this point, but DK/T values for the different lens materials being used, so clinicians can determine where they are prescribing lens for overnight wear that it meets the Holden-Mertz criteria.

Do we want to do one at a time?

DR. WEISS: Yes, why don't we do one at a time, and if there is any disagreement with those, so then we can just include them as a final list later on.

Dr. Harris.

DR. HARRIS: I don't disagree at all with the inclusion of a table or a list. I question whether the list should indicate that one of the materials meets the Holden-Mertz criteria and the other doesn't.

DR. McMAHON: That was not to be included, it was just a reference for those who may not know about Holden-Mertz criteria.

DR. HARRIS: Well, that is the point I am trying to make. How are we educating patients and/or practitioners about these two materials if

we don't let them understand why we are indicating the DK's of the two different materials, we are not just doing it because we want to see those numbers in print, we are doing it because we think those numbers have some importance and the fact that the material with the higher DK, based on studies that have been done for a number of years, is one that is considered meeting the minimum oxygen requirements for overnight wear, and the other one doesn't.

The idea of labeling is to inform consumers, so that they have information that they can use to help them intelligently decide whether or not this is an appropriate product or whether they are getting the right product.

I would like to see, if we are going to include these numbers, which I think we should, that we recommend labeling that does also indicate why these numbers are important. It is a brief statement.

DR. WEISS: Is this the standard in contact lens labeling, Dr. Saviola? I mean I don't know that it should be the sponsor's duty to educate patients as far as other lenses, and such. If you could guide us.

DR. SAVIOLA: I am trying to recall how often it has been noted. I can't off the top of my head cite it. It was a critical factor in the approval of the 30-day lenses, and it has been a factor that we have used in IDE studies for lenses beyond 7 days.

In this situation, I think we have used it as just a notation, like a footnote to the reference to the 1984 article is what we might have.

DR. WEISS: Dr. McMahon.

DR. McMAHON: I am one of the few people who actually reads contact lens labeling.

DR. WEISS: There is one in every group.

[Laughter.]

DR. HARRIS: Get a life, Tim.

DR. McMAHON: That means I have to go off the panel.

There are so few lenses that meet the Holden-Mertz criteria that no, it hasn't, except that I think it is in the labeling relative to the silicon hydrogels, but there is so few that meet it, I don't think it's the standard. That doesn't mean it is not important.

DR. HARRIS: I just raise the issue. If

we are going to ask the sponsor to indicate the DK/L of these two different materials, we are doing so because we think it is important that somebody understand the difference between these two numbers.

If we want them to understand the difference between these two numbers, we have to give them some additional information so that they can make a rational judgment about the various numbers.

Either leave out the information about DK/L altogether because you think the two materials are equivalent and it doesn't matter which material a particular patient gets, or if you think it is important that they get a certain material under certain conditions, let them understand what those conditions are.

DR. WEISS: The question is, is this for the practitioner or is this for the patient?

DR. HARRIS: The labeling goes with the lenses, so the practitioner is responsible for understanding the labeling because it is their responsibility to know the material that is in any package label, and the labeling is also important for a patient to make intelligent decisions about

whether or not this is an appropriate product for them and they are getting the right particular lens design material, or what have you, for their needs.

DR. WEISS: We should make sure we are not going to be any more burdensome for this sponsor than we are for anyone else, but I would like the panel to reach some consensus and discuss this.

Dr. Smith and then Dr. Grimmett, please.

DR. SMITH: We did say that because of the fitting requirements of this lens, that there will be a physician or eyecare provider educational component, which is different from other contact lenses, and this is information that could be included in a physician's information booklet, and may be more appropriately inserted there because a patient doesn't really have the ability to interpret whether it complies to any rules anyway.

Since we don't have specific data saying you should exceed this value if you have this condition, it would be premature to include that in information that is given to patients because they can't interpret that.

DR. WEISS: Dr. Grimmett.

DR. GRIMMETT: I would like to voice support for the comments of Mike Harris. We are

talking about an overnight circumstance in which hypoxia is an issue, and I think giving a practitioner in a physician information booklet the baseline information to understand what DK information means is relevant to those tables for the information we are trying to communicate.

I don't find it burdensome at all to include the basis for why we are including the tables.

DR. WEISS: Dr. Van Meter.

DR. VAN METER: But hasn't this lens already been approved for extended wear?

DR. WEISS: Yes.

DR. VAN METER: So, I mean we are already beyond the DK issue for nighttime wear. I guess my question is I understand your intent, but would that not be overly burdensome? I think the sponsor has already jumped through that hoop.

DR. WEISS: Dr. Harris.

DR. HARRIS: But we are going one step further with this. If we follow through with the discussions earlier, we are going to ask that there be some additional training and a practitioner fitting guide, so to speak, and certainly the practitioners need to understand the differences

between the two materials and making rational choices as to which material to use, with which patients, under which circumstances.

DR. WEISS: I think there is probably consensus in terms of the practitioner having the information. I think what we were discussing at this point is should the patient have the information in the insert with an explanation of what the information means.

I see a no. Dr. Casey and Dr. Smith seem to be shaking their head no. Okay.

So, there is agreement on the labeling issue No. 1 on Dr. McMahon's list, is that this would be information provided to the practitioner, but not to the patient.

Would you be able to continue along with your list?

DR. McMAHON: No. 2 is efficacy and safety in non-Caucasian eyes may not be similar to the results presented in this PMA study. This pertains to the issue of the vast, vast, vast majority of patients were Caucasian, and there is some circumstantial evidence published that indicates that other ethnic groups have different corneal geometries, and actually new data suggests actually

epithelial permeability may be different, but that is a separate story.

For example, I have no idea whether this works in Asian eyes. I don't think we should preclude folks with non-Caucasian eyes from being fit with this lens, but there may be an advisory statement in the labeling indicating that the study did not look at those groups.

DR. WEISS: Dr. Smith.

DR. SMITH: I agree with Dr. McMahon. This is something that patients can interpret, and I would suggest that it should be included in both the physician and the patient information.

DR. WEISS: Dr. McMahon, if you could continue.

DR. McMAHON: No. 3 is include the dropout rate found in the PMA. It's 34.6 percent.

DR. WEISS: Would there be agreement that would be in both physician, as well as patient information? Dr. Harris.

DR. HARRIS: I agree wholeheartedly, but I also think that that table should also include the success rate. Dropout is one thing, success is another, and I think it is important that both practitioners and patients understand, not only the

likelihood that they will not continue wearing this lens, but the likelihood that they will meet certain criteria of success.

DR. WEISS: We will add that as Point 11 in the list, because there will be additional labeling issues in addition to the ones that Dr. McMahon has already listed.

Can you go on with No. 4?

DR. McMAHON: Safety and efficacy in children under 18 years of age has not been determined. I would like that added to both the physician's and the patient label.

That data, although there were some individuals between 12 and 18 included, the volume of those was very small, and actually, I think the majority of those individuals dropped out and had less than nine months data, so I don't think that is interpretable.

DR. WEISS: Dr. Harris.

DR. HARRIS: I agree with the sentiment of this labeling, but I would to raise an issue to go even beyond that, and I haven't reached a conclusion on this yet, but just to raise this.

Those folks under 18 are a vulnerable population. They do not have the ability to make

these kinds of medical decisions on their own, and their parents have to make them on their behalf. The question is whether or not we have sufficient data to indicate that this is a safe and effective procedure for people under the age of 18.

One way to handle it is by virtue of this kind of labeling that Tim has indicated. Another is not to approve it for use under 18. While I recognize from a clinical standpoint that a large percentage of the people who may be interested in this are parents who have teenagers who are becoming more myopic and they want to use this as a method of care, I would like to have every member of the panel consider whether or not they think it is appropriate for this modality to be used on people under 18 given the information that we have at hand.

DR. WEISS: Any comments, discussion on this?

DR. VAN METER: I agree with that and would go so far as to say I would support not approving it for use under 18. People that are teenagers and wear contact lenses really don't make very good judgments about the health of their eyes, and safety and efficacy is lost on them.

I would exclude the use of the lens in people under 18.

DR. WEISS: Dr. Matoba?

DR. MATOBA: I agree.

DR. WEISS: Dr. Harris?

DR. HARRIS: I am just saying I agree with myself.

DR. WEISS: I am comforted by that fact.

Dr. McMahon, can you continue with your list?

DR. McMAHON: Did we decide on that?

DR. WEISS: I had three indications that the panelists wanted to have the approval for 18 years or older, and have this taken out of labeling because it won't be an issue if it is not approved for it.

Do you have any other thoughts on it?

DR. McMAHON: Yes, I read what my thoughts were.

DR. WEISS: Well, you are consistent again, too. So, let's go to No. 5.

DR. McMAHON: My point is that you have a minority of the panel suggesting --

DR. GRIMMETT: We will make a motion and vote later.

DR. WEISS: Is there any disagreement with that, why don't we put it that way? No disagreement, so let's move on to No. 5.

DR. McMAHON: All conditions excluded from the trial should be defined in the labeling. As I mentioned in my brief talk, there is some discrepancy between those who are excluded from the trial versus those that are excluded in the labeling. I think they should be consistent or at least accounted for.

DR. WEISS: If there is no discussion on that, we will go on to No. 6.

DR. McMAHON: Include Table 9, page 57, in the labeling, which has to do with treatment or the equivalent of my slide 15.

DR. GRIMMETT: To refresh everyone's memory, that is the post-treatment uncorrected visual acuity stratified by manifest refraction spherical equivalent in patients who are targeted for emmetropia.

DR. WEISS: This would just sort of get back to Dr. Harris' comment in terms of success rate. Is that what you were referring to, a success rate, or you wanted more than that?

DR. HARRIS: No, I think that will

suffice, and I urge the sponsor and the agency to use a table more similar to Dr. McMahon's than the one published on page 57 if you want people to truly understand what their likelihood is of success.

DR. McMAHON: I can make a copy of that.

DR. WEISS: No. 7?

DR. McMAHON: Include a statement that CRT appears not to affect pretreatment astigmatism. I think that may actually be in the labeling already.

DR. WEISS: If it is not, then it can be. Would there be anyone while we are doing this that can check the labeling to see if that is already -- Dr. Matoba, would you be so kind as to check the labeling to see if that statement is in there? Thanks.

No. 8?

DR. McMAHON: Include a table post-lens removal treatment effect by time including 8, 16, and 24 hours. They have 8 hours, they have 24 hours, as Dr. Edrington had mentioned, that nighttime number is not there. If the sponsor has that, I think that would be important to have.

DR. HARRIS: Excuse me. That should be indicated by refractive error, initial refractive

error, as well, because there is a significant difference based on -- stratified by refractive error -- there is a significant difference based on whether the individuals are low myopes or moderate myopes to begin with.

DR. McMAHON: That would be my intention. I support that.

DR. WEISS: No. 9.

DR. McMAHON: It is that time to baseline should not be spherical equivalent. Best corrected visual acuity after discontinuing treatment should be defined. At this point, the sponsor has provided data with regard to the first three days, and as I have mentioned, that time frame is likely to extend out further with somewhere in the neighborhood of a 43 percent dropout rate.

I think practitioners and patients need to know what their time to pretreatment visual recovery is going to be.

DR. WEISS: No. 10.

DR. McMAHON: The transient changes in post-treatment best corrected visual acuity should be defined in the labeling. This, Dr. Matoba has also mentioned.

DR. WEISS: How does that differ from No.

8? Are you talking about the 4 percent of people that lose best corrected vision?

DR. McMAHON: Right.

DR. WEISS: How about making that a table of the side effects including the fact that 75 percent of patients have discomfort?

DR. McMAHON: You mean initially?

DR. WEISS: Well, a percentage of the side effects noted with the lens, or you just wanted -- the transient changes you were referring to --

DR. McMAHON: The same ones that Alice mentioned, the certain group of individuals that seem to have, but appear to be transient, changes in visual acuity. They are not defined at this point in any concrete nature, but certainly somewhere along the line some people have some difficulties, and that should be defined.

DR. SAVIOLA: Dr. Weiss, may I ask a question for clarification?

DR. WEISS: Yes.

DR. SAVIOLA: In your comments regarding No. 7, astigmatism, and No. 8, post-treatment post-lens removal and the effect thereof, if you refer to page 177 of your package, which is a CRT, there is a section there entitled "Duration of myopia

reduction that goes out 72 hours post-removal and effects on astigmatism," and my question is do you feel that these sections are inadequate or are they addressing your questions No. 7 and No. 8?

DR. McMAHON: Labeling on 139, astigmatism, I think is fine.

DR. SAVIOLA: You are on page 139? I was on 177.

DR. McMAHON: I don't think 72 hours is long enough.

DR. WEISS: Page 177, wouldn't that address more than sufficiently Point No. 8, because 8 hours, 24 hours, 48 hours, and 72 hours post-removal?

DR. McMAHON: Sixteen.

DR. WEISS: I see, you want the interim when you are driving home from work.

DR. McMAHON: One is intra-day and one is what happens if you decide to get out of the game all together.

DR. WEISS: Very good point. Any other labeling issues? Dr. Bradley.

DR. BRADLEY: I was intrigued by the discussion of teenage behavior. My son is about eight years away, so I have at least eight years to

study up on this, but it reminded me of an issue of compliance, and I will just give you a scenario.

Imagine when you have a minus 6 optimyo who is undergoing nighttime treatment, and the treatment is completely effective, and they wake up plano. On one particular night, for whatever reason, they may have forgotten to put their nighttime lenses in, and they don't wake up plano or minus 6, they wake up minus 3.

What is that patient meant to do? I wondered if the contact lens people might be able to give some suggestions because they can't wear their spectacle lenses, which are minus 6's, and they can't wear nothing, because they are minus 3 diopters myo.

DR. HARRIS: A very good question.

DR. BRADLEY: The reason I raise it now is it seems to me that might be a significant issue to put in the labeling, to warn patients that failure to comply with their treatment regime could produce this odd result.

DR. WEISS: I think the sponsor had an answer to that.

DR. MEYERS: Put on their contact lens.

DR. WEISS: But as it is changing -- I

have the same question -- when they are driving, after eight hours, and it starts to degenerate after the eight hours --

DR. MEYERS: Put on your contact lens and you are back to the corrected version. Regardless of what the cornea is doing, the tear lens is making the change as you go through the day.

So, anytime you put your lenses on, you will get corrected vision.

DR. BRADLEY: Let me just clarify then. This strategy you have just explained would work for a patient who is a contact lens wearer. I am thinking about a patient who may be a spectacle lens wearer, is undergoing this treatment, what would they do.

DR. WEISS: If the sponsor could just his answer in the microphone, so we have it for the record.

DR. MEYERS: He would put in his treatment lens.

DR. BRADLEY: Did you say the treatment lenses are all plano?

DR. MEYERS: Yes, but the tear lens underneath it is not.

DR. WEISS: Dr. Harris.

DR. HARRIS: Theoretically, the sponsor is absolutely correct. If the lens is designed in an appropriate fashion, and the amount of flattening of the lens matches the amount of myopia, you have a tear lens that is going to correct the patient's refractive error even though the patient has a planar lens, so in theory, they could put on their treatment lens and be able to see.

The problem is that that is not one of the indications for this lens. It is not indicated for daily wear. So, if that is a solution to this potential quandary that Arthur has raised, we need to make sure that we make some statement in labeling or indications that the lens may be worn on a daily basis if necessary to maintain proper vision.

DR. BRADLEY: I agree. I think the sponsor has given the correct answer. I was raising it because it seemed to me that that must be put in the labeling, the strategy for the patient.

DR. WEISS: We probably need to then, I go back to sponsor and find out what you have been doing with these people whose vision gets blurry on the road at 5:00 p.m., especially if one of them is

driving next to me.

I don't know, if the sponsor could come up again and effectively, are you telling these folks when they leave work, to be putting on their lenses, or is it not an issue because the vision is still 20/30, or by the time they get home, that is when the vision starts to fade?

DR. LEGERTON: There was an amendment to the protocol that allowed the practitioner, the investigator to deliver a soft lens, disposable soft lens, that could be used from time to time. That was particularly important during that first 30 days. A patient could be told just don't drive, which I think is what we do in refractive surgery while someone is adapting or whatever, if it's not in their good judgment, they don't see, don't drive, but that is not practical for all people.

What was done in this case, if the practitioner felt that there was a need to set something intermediate to their prior spectacle or contact lenses, and did not, they were instructed to not wear this lens during the day even though they could, and they could see with it, that then they would use a hydrogel lens as an intermediate step.

This, I believe is something that should be handled in labeling, to say that there are times that in the regression of effect, that you may not have full acuity to perform all of your daily tasks, and that there are alternate methods of correction during that time.

DR. WEISS: For the panel, maybe we can just wordsmith it or perhaps that should be discussed with your practitioner, so the practitioner can get involved in how it gets done.

DR. WEISS: Two other labeling questions that I had. One was the high altitude, which I don't know if it is on the list just yet. Is that on the list?

DR. GRIMMETT: Yes.

DR. WEISS: That is on the list. Okay.

The other thing is I wanted personally to have the panel think about having something in there about side effects, especially the 75 percent discomfort rate, which to me is something that someone should know about before they get the lens.

I see some agreement with that, so that could be put in there. Any other additions on the labeling? Dr. Harris.

DR. HARRIS: Just to clarify what Arthur

has said. I think that the labeling needs to clearly state that in order to maintain the effect, the lenses need to be worn every night overnight.

DR. GRIMMETT: That is in there already. Dr. Edrington made that in his presentation. That is in there already.

DR. WEISS: I am not sure, this may not fit into this question, but as long as we are discussing these things before we go on Question 5, I will bring it up.

It is the training that was previously discussed, what would be the feeling of the panel as far as what should be requested for practitioner training? Dr. Harris.

DR. HARRIS: Well, I haven't given it a lot of thought, but similar to the kind of training that we indicated years ago when we approved refractive surgery, that the sponsor was responsible for putting together a fitting guide and manual, and making sure that practitioners who used the lens understood all the various nuances in fitting. Whether we want to have some kind of certification or not is a separate issue, but certainly practitioners need to have a fitting guide and need to understand how the lenses work.

The sponsor indicated in the presentation that the fitting was a really important factor in achieving success and efficacy, and with that in mind, obviously, it is in the sponsor's best interests to make sure that practitioners are well qualified when they use this particular material and design.

I think that the agency has an obligation to make sure that individuals who are using this are qualified to do so.

DR. WEISS: I would assume there would probably be consensus with the written guide. Is there any feeling about an actual training course or anything more involved, a video, whatever? Dr. Edrington.

DR. EDRINGTON: I believe currently there is, that they are doing workshops and such for fitting. I am not sure a guide is going to make a practitioner proficient in the fitting of this lens. I believe currently, to utilize the lens, you have to have been certified or go through a workshop or training session.

DR. WEISS: But that may be part of the clinical protocol. The question is afterwards, would you want that to still be a requirement.

DR. EDRINGTON: Based on what I understand, there is a higher level of proficiency necessary to fit this lens. If nothing else, there is a need to understand the terminology. It is a little different terminology than what we are used to using, as well. So, I would highly recommend that there be a training session, that a person be certified to fit this lens.

DR. WEISS: Dr. Bradley.

DR. BRADLEY: Another potential issue for labeling, again, I would seek the counsel of the contact lens practitioners here. One thing that wasn't clear to me in the way that this lens would be implemented in practice is what would be done if the patient was what I would classify as a failure, one of these 10 to 15 percent who didn't achieve 20/40 uncorrected visual acuity.

Should something be placed in the labeling, I think in this case to the practitioner, indicating responsibility to inform their patient that they have what we might consider substandard acuity or give them some indication that their acuity does not allow them to drive safely, et cetera, because it looks like a significant proportion are going to be in this group.

That raises the more general issue of will the clinician be responsible for evaluating the success of the therapy on the patient. Again, it comes back to how, in clinical practice, these lenses will be used.

DR. WEISS: Dr. Edrington.

DR. EDRINGTON: Just a follow-up in terms of the training and such. I would think -- and maybe this is a burden on Paragon for us to request training, but it seems it would be in both Paragon's best interests and the success of this lens' best interests that if practitioners out there that don't know how to fit, they decide to dabble in it, and have failures, that is going to get out and it is going to harm the product in the long run.

So, I am saying it in a way to help the sponsor as opposed to putting another burden upon the sponsor.

DR. WEISS: Dr. McMahon.

DR. McMAHON: On two issues. One, I support Dr. Edrington's comments. The sponsor has already demonstrated this prior to even seeing this panel. They are out educating individuals, and it is in their best interests, and I don't think we

need to burden them with that. They already realize this is in their best interests, they want to make this a success, and I think that they know that they are going to have to train clinicians.

DR. WEISS: So, you would recommend not leaving it up to the sponsor to make that decision?

DR. McMAHON: That is correct.

The second is with regard to Dr. Bradley's comment with regard to informing patients. That gets into best medical practice issues, and I would leave it there.

DR. WEISS: Dr. Harris.

DR. HARRIS: I agree with both what Arthur and Tim said. Now, you are going to ask me how the heck can I reach that conclusion. Arthur had an eloquent solution to the problem where patients were not seen properly in the morning, and that was the fact that they needed to be advised in the product labeling that if their vision is not appropriate, that they may need to have some additional correction, they should consult with their eyecare practitioner to determine what correction is necessary.

That same kind of labeling could apply to people whose vision is not at an acceptable level,

and the labeling can simply state that some individuals may not have satisfactory vision after treatment, and in those cases, supplemental eye correction will be necessary, and you need to consult with your eyecare practitioner as to how best to solve that problem.

DR. WEISS: Sounds good to me.

Dr. Rosenthal, did you have a comment?

DR. ROSENTHAL: I think I really need the sense of the panel's recommendation concerning a formal training program, please.

DR. WEISS: Dr. Edrington, do you feel that a formal training course should still be required of the sponsor?

DR. ROSENTHAL: Excuse me. Mainly because, you know, this is the first of a kind, and we are setting a precedent for all other companies, and if you ask it for one, you will ask it for all, if you ask it for none, you will ask it for none.

So, I really need a sense from you all.

DR. EDRINGTON: In one respect, I almost think Paragon would like for us to put that in there because then it would be an answer to practitioners saying I just want the lens, I don't want to go through your training course. They can

just say we are required to by FDA.

But in thinking over what Dr. McMahon said, again, I think Paragon will continue to do the training just to be successful with the product, but maybe we should not put that stipulation upon them.

DR. WEISS: Dr. Smith.

DR. SMITH: I think there can be a middle ground between that. There are a variety of things in the government, for example, there are computer based training and certificate programs that government employees have to do, I have to do like five of them every year on specific areas.

So, I think there is middle ground between that. For example, we could recommend that the FDA require the company to provide a videotape, which is a videotape of one of the training programs or we could recommend that the FDA require the company to have training programs over the next two years at specific interval at specific sites.

DR. ROSENTHAL: The FDA can mandate training, but it does not mandate the type of training. I don't want to get into the FDA dealing with what type of training. As we have been through with excimer lasers, it has been a very

controversial issue which the panel recommended and which we were able to uphold because of the panel's recommendation.

I would like a panel recommendation on whether or not they feel a training program is appropriate, and I think the agency will then determine and work with the company to come up with what components of that training program is appropriate, and then how it is done is very much going to be left up to the company, whether they do it, whether the video does it, whether they have people do it, blah-blah-blah.

DR. WEISS: Dr. Saviola.

DR. SAVIOLA: I just wanted to make note on Ralph's comment for clarification, that we do have sort of three choices in terms of restricting a device under Class III. One is to prescription use, one is restriction for advertisement purposes. We applied those two to the 30-day contact lenses. The third restriction is for training, which you have applied in other devices in the past.

So, as Ralph says, if you restrict this one, you say this can be sold only to those practitioners who have received training, and we are not defining what that is. Then, we will carry

that forward for other types of devices of a similar type.

I am sitting here wondering. I know you haven't really resolved the decision between the CFT design versus the Quadra RG, but I am sitting here wondering, because of the complexity of the way the sponsor described fitting them with CRT, would this recommendation for training apply to both designs if you indeed recommend approval for both designs.

DR. WEISS: I will throw that to the panel, but my assumption is there is no reason why one would assume one was easier to fit than the other, so I think it would apply to everything that would get approved.

Dr. Harris.

DR. HARRIS: I think training is appropriate with this particular indication. I think it is in the best interests of the sponsor, it is in the best interests of practitioners, and it is in the best interests of the public that we serve.

DR. WEISS: Dr. Grimmett and then Dr. Smith.

DR. GRIMMETT: I was going to make the

same comment that Dr. Harris made. I do not fit ortho-K lenses, but I am hearing from my colleagues here, who fit these lenses, that it does require a higher level of expertise, and it is not standard, routine contact lens fitting.

It is my opinion, therefore, that a training program is appropriate and should be mandated.

DR. WEISS: Dr. Smith.

DR. SMITH: I agree with both Dr. Harris and Dr. Grimmett.

DR. WEISS: Dr. Edrington.

DR. EDRINGTON: Just a point of clarification. I think the CRT design is a unique design at this point in time. I think if the Quadra lens is sort of a more standard type -- sorry to use this word -- orthokeratology lens, a lot of the practitioners have experience in that area, and that product has been around for a while, has been hopefully trained a little bit in some of the schools, so as a new CRT design, I assume down the road, as practitioners become more familiar with the terminology and the fitting techniques, as is taught in educational programs and that, it might not be quite as important in the future, but

currently, I think it is a unique fit and to succeed, does need training.

DR. WEISS: So, would you propose indicating that training would be required for the CRT, but not for the Quadra?

DR. EDRINGTON: I probably have a question myself in terms of the Quadra design. Am I missing something in terms of thinking it is a reverse geometry lens and --

DR. WEISS: Could sponsor comment, is there a major difference in terms of fitting one or another in terms of difficulty level? I would ask sponsor to come up.

DR. MEYERS: There are certainly nuances of fitting either one of these lenses that are different than fitting standard rigid gas permeable lenses. I think there are practitioners who have practices with reverse geometry lenses that don't have it with CRT, but I think they are also few and far between.

If this is going to become a universal modality, I think training in Quadra would be equally required for appropriate use of the lens. So, I think if it's one, it should be all.

DR. WEISS: Thank you for your candor.

Dr. Edrington.

DR. EDRINGTON: Just to bring up a side issue, that I am not sure how it is handled. A lot -- I won't say a lot -- but reverse geometry is also used to fit like post-surgical cases, it is used to fit traumatized corneas, irregular corneas, and such.

So, would this mean the doctor would have to go through the -- is this just for the use of orthokeratology or would a doctor have to go through this program to use it?

DR. WEISS: I think it is for the lenses being approved for orthokeratology. Now, the question is would you not be able to buy the lens unless you did the training, and if you wanted to use it in an off-label use, but I don't think that is our purview to discuss.

Dr. Rosenthal? Fine.

Any other questions? Yes, Dr. Matoba.

DR. MATOBA: We are still on labeling?

DR. WEISS: We are still on labeling if you have anything else for labeling.

DR. MATOBA: Yes, I have a question. For this particular indication for the lens, should we consider listing alternative therapy in the patient

information booklet?

DR. WEISS: Dr. Harris.

DR. HARRIS: Alice raises an interesting question. I was going to raise it as a more generic question, and that would be a discussion of whether some kind of an informed consent document is appropriate with this particular indication. An informed consent document would include many of the things that we have indicated in the labeling, and in addition, would include alternative therapies and likelihood of success.

DR. WEISS: I would think that would be burdensome personally, because this is not a surgical device, and the risks were very, very small, so I don't know why you would need informed consent.

Dr. McMahon.

DR. McMAHON: To address Mike's comment, I think that would be under again the best optometric, best medical practice decision process rather than FDA, but did we actually answer your question, Ralph, about training?

DR. WEISS: Yes, I think. The feeling that I got from the panel is that they wanted training. Does that answer your question? Okay.

Dr. Grimmett.

DR. GRIMMETT: I will defer to Dr. Harris given his degree in law, however, based on my experiences as a medical expert witness, it is my current belief that informed consent is a process, and not really a form, hence, the patient information booklet and any other information they garner during the process of evaluating a device could be construed as informed consent.

I would think that if all the information is included in the patient information booklet, that that would be sufficient for informed consent.

DR. HARRIS: The reason I mention is because in one of the reviews, I believe it was Dr. Edrington, he mentioned some consideration of whether a specific informed consent document would be appropriate with this particular device. I just wanted to raise that issue for clarification.

As we are talking about labeling, it does fit in with labeling, and I just wanted to find out if that was the consensus of the panel or not.

DR. WEISS: Dr. Van Meter.

DR. VAN METER: The alternative to this is that the patient can just remove the lens, and I believe the patient is free to remove the lens at

anytime. The information we have is that the eye pretty much goes back to normal, and I would agree with Mike, that I think informed consent of the document would be helpful, but I don't think there needs to be -- there doesn't have to be an informed document to sign. I think if we give the patient sufficient information, the down side risk is really pretty low.

DR. WEISS: I would bring up one other question to the panel. Although there were no corneal infiltrates reported in this study, with larger numbers, there is a decent possibility someone is going to get a corneal infiltrate, I would think.

Is it worth saying a statement to the effect that none were reported in the study, but it doesn't rule it out in the future? You are shaking your head, Dr. Harris, do you think it should be left out?

DR. HARRIS: Well, there are all kinds of things that didn't come out in this particular study, that contact lens patients can and will have happen to their eyes while wearing contact lenses, and obviously, there need to be the general warnings that if you have of these kinds of adverse

symptoms, red eye, decrease in vision, discharge, you need to see an eyecare practitioner.

DR. WEISS: Dr. Matoba.

DR. MATOBA: My question was should we list alternative therapies in the booklet.

DR. ROSENTHAL: I would appreciate the panel's sense of that, please.

DR. WEISS: What is the feeling about listing alternative therapy?

DR. McMAHON: This is a new arena. It is not typically done in the contact lens realm at all. However, we are kind of in this between land, between refractive surgery and conventional contact lens.

DR. ROSENTHAL: It is done in the refractive surgery realm.

DR. McMAHON: I said in the contact lens realm.

DR. ROSENTHAL: I am sorry.

DR. McMAHON: Refractive surgery, I know it is, but those are also permanent procedures, most of them are.

[Laughter.]

DR. McMAHON: I wouldn't oppose it, but it is definitely sort of cutting new ground to do

that.

DR. WEISS: Dr. Harris.

DR. HARRIS: It is reasonable and appropriate to include it, but just a simple statement in the labeling.

DR. WEISS: Dr. Grimmett, do you want to wordsmith that?

DR. GRIMMETT: Well, a comment first. I do think it is reasonable to include alternative therapies in the patient information booklet, because a patient considering this type of therapy is being bombarded with advertising on refractive surgery and other matters.

I certainly think in terms of a well-informed patient making a reasonable decision whether or not to undergo a treatment such as orthokeratology, it is reasonable to list spectacles, other refractive surgical techniques, and so on, and so forth.

DR. McMAHON: Contact lenses.

DR. GRIMMETT: Contact lenses, daily wear, same thing, all those issues.

DR. McMAHON: Or extended wear.

DR. WEISS: Dr. Coleman?

DR. COLEMAN: I agree with listing the

alternative therapies, and in addition, I was thinking it is important to mention that the individuals who go through the orthokeratometry have very similar success rates or happiness in terms of their vision as they did with their habitual correction, because it was about 93 percent at the start, those individuals with habitual correction, and then nine months later, it was about 91 percent reported excellent or good vision.

I think it is important to realize that they are not going to have any better vision, not necessarily any more happiness with their vision with the use of these devices.

DR. WEISS: Are you proposing that that table of satisfaction be included in the patient information book?

DR. COLEMAN: Yes, or a comment, maybe not a table, but just a comment that it was similar.

DR. WEISS: Any other labeling issues? If not, we will go to Question No. 5.

What are the panel's recommendations regarding post-approval follow-up of the study subjects or a post-approval study of corneal warpage effects over time?

Dr. Edrington.

DR. EDRINGTON: I think the longer follow-up, again, I think the treatment effect was shown pretty nicely, but longer follow-up to maybe help address patient questions regarding long-term stability of treatment effects, and also corneal warpage.

I was a little unclear. Topography data was collected, but not analyzed, or not collected?

DR. GRIMMETT: Collected. Dr. Bullimore indicated it was collected, but different facilities used different topographers, and it was difficult to analyze due to lack of standardization.

DR. EDRINGTON: But each of those instruments probably puts out some sort of regularity type index or indices, and it might be interesting to share that with the FDA, especially long term, to see if there is any corneal warpage over time as such, but that would be my only thoughts.

DR. WEISS: So, you are talking about post-market surveillance?

DR. EDRINGTON: Yes.

DR. WEISS: Again, we want to stick to the

least burdensome, and if there is a danger that you think that we may not be detecting, then, we can be doing that, but if it is more for a matter of academic interest, then, that is really up to the investigators and people in the academic and private sector to write the articles on the issue and leave the FDA out of it.

Dr. Harris.

DR. HARRIS: If the panel goes forward and approves both lens designs, since no data was supplied with the Quadra lens in the intended use, is it appropriate to have a post-approval study on that design?

DR. McMAHON: I think the panel said that the other design was not going to be considered.

DR. HARRIS: No.

DR. WEISS: By a vote of one, Dr. Matoba, at least as of the last polling, it was going to be considered. She was the swing vote. It was 5 to 5, and then Dr. Matoba went to the other side, or one side.

Dr. Bradley.

DR. BRADLEY: I am not sure we have seen any significant safety issues or any significant regression of effect in the data that has been

presented, and I find it difficult to therefore justify requiring the sponsor to collect more data, and unless we can come up with some reasonable belief that there is some genuine concern for safety that may appear after nine months, or that efficacy is somehow eroding and we want to see if it continues to erode, I think we should not require it.

DR. WEISS: Sally has just brought this to my attention. In Dr McMahon's review, he felt that there was an omission in the PMA in the time to recovery after treatment, not being totally elucidated.

Does anyone else have this concern? Do you still have this concern or less so?

DR. McMAHON: Oh, yes.

DR. WEISS: You still have this concern, okay.

DR. McMAHON: The point of this being that individuals, again, in the study, 43 percent of so, the individuals end up discontinuing treatment, and we don't know the time to baseline visual acuity and baseline manifest refraction.

We have three days' worth of data, which for the individuals that have high refractive

error, usually, their recovery seems to be within that time frame, but those with lower refractive errors had relatively little change within that time frame, so we don't know what that duration is, and therefore, you, as practitioner, aren't going to know how to advise your patients when you are going to get back to where you were.

DR. WEISS: Dr. Edrington.

DR. EDRINGTON: Just to follow up on my original statement, I think it would be interesting to see some of these indices in terms of regularity, and to see the changes over time. If they took the data, they have the data already if they have taken it each visit to see if there is changes over time or if it stabilizes out.

I agree with what Arthur said in terms of we have seen sort of in one sense, the long-term safety and efficacy of the procedure, but it would be interesting to see if we are changing the cornea in terms of distorting the corneal surface over time.

If that data followed the data of the refraction, followed the data of the keratometry, I would have no concerns.

DR. WEISS: Does anyone else have this

concern? Anyone else interest in post-market surveillance?

Dr. Ho, I see you shaking your head in the negative.

DR. HO: I think that in the spirit of least burdensome, but really, it would be nice to know over time to be able to advise our patients, or advise potential patients now, but I think these are things that will be borne out over time with experience with the lens, and can be published academically, and not necessarily the requirement here that we can mandate that.

DR. WEISS: Dr. Edrington.

DR. EDRINGTON: I would say it doesn't need to be longer follow-up unless data like that -- I think that data would just be interesting to see for the FDA, to see if there is a trend, and then there be longer follow-up. I seem to be the only one that has that interest, though.

DR. WEISS: Dr. Bradley.

DR. BRADLEY: I think I could much more easily vote on that particular issue if I could see some data. I am looking at a table which shows how acuity changes up to 72 hours post-removal.

Do we have data or were we given data on

how refraction changes? That is the question that I think is floating around here, because if the refraction had returned to its original level at 72 hours, then, we don't need any more data. I just didn't see those data.

DR. WEISS: The sponsor can come up and answer that, please.

DR. LEGERTON: The post-removal, 8, 12 or 24, 48, 72-hour visits did require keratometry and manifest refraction, so that can be analyzed. It was not analyzed for the submission. One of the other requirements was, though, to follow discontinued subjects until they returned to baseline. At the request of Dr. Schein, we evaluated the cohort that had had at least four weeks of treatment, so we wouldn't be biasing it by people that had just one night of treatment.

Of the 142 eyes that discontinued -- can't do it?

DR. ROSENTHAL: I am sorry, it is inappropriate to provide information that wasn't in the PMA, but it would be important for the panel to know whether or not you can provide that information.

DR. WEISS: What we can do is if this is

information that is important, you can request that the sponsor provides it, and they obviously have it.

DR. BRADLEY: Again, regarding a vote on post-market study, I am thinking that if these data already exist, and you can provide them to the FDA, and convince the FDA all the recovery in terms of refraction, then, those data should be in the labeling, so that both the clinician and the patient can understand the time course over which they can expect to return to their pretreatment refraction. We have not seen those data.

DR. CASEY: Dr. McMahon.

DR. McMAHON: If the sponsor has this information and if the sponsor can demonstrate that the discontinued group is not significantly different from the continued group in their behavior, I would be very happy with them just supplying that information, adding it to the labeling, and not having any post-market studies.

DR. WEISS: Would you have consensus on that, Dr. Edrington?

DR. EDRINGTON: Yes.

DR. WEISS: Fine. It sounds like the sponsor has this information, so that we can add

that to that, that that information will be required.

Any other additions on this question? Seeing none, we will proceed to Question 6.

Do the data presented in this PMA provide reasonable assurance of safety and effectiveness for the proposed indications? Dr. Harris.

DR. HARRIS: As stated earlier, I believe the data do support with reasonable assuredness the safety and efficacy of the CRT lens. I still question the safety and effectiveness for the indicated use of the Quadra lens because there has been no data submitted to show that.

I am somewhat confused as to what the consensus was in the various straw polling that we did earlier as to how this particular Quadra design is going to be viewed by the majority of this panel.

DR. WEISS: That was more for my edification to see which way it was going to go, but that's not a final vote, and until the final vote, anyone can change their opinion as to which way anyone goes. It was close.

DR. HARRIS: Based on the data submitted, again, there is reasonable assurance of the safety

and efficacy of these CRT. I question whether or not that same assurance, reasonable assurance is there based on the lack of information presented in the indication under submission.

I recognize the fact that there may be some implications from other uses of this particular design, but there has been no indication of the safety and efficacy in this design. That is the only issue that I have to struggle with in providing my final vote.

DR. WEISS: Any other responses to this question?

[No response.]

30-Minute Open Public Hearing Session

Seeing no responses, we will then move on from the panel discussion to the 30-minute open public hearing session, if there is anyone who wants to make any comments.

[No response.]

DR. WEISS: Seeing no one, we will then go on to FDA closing comments.

Dr. Saviola.

FDA Closing Comments

DR. SAVIOLA: I would like to just make one comment in regard to the CRT Quadra dilemma we

seem to be faced with, and try to distill it down into the essence of the discussion, the decision point here.

Within the body of all of our contact lens guidance documents we have available, we pretty much allow firms to make variations on certain geometries of the standard lens design in terms of overall diameter, base curve radius, peripheral curve geometry, et cetera.

That guidance was something that with the history of rigid lenses being run since the sixties, has been in place for a number of years.

The question before you folks today, and again, you can appreciate the difficulty in trying to answer this with this new technology, first of a kind consideration, is how much do you feel comfortable as an advisory group endorsing that type of concept in this particular type of lens design, because the device itself is actually a combination of the material and the design. So, we are really talking about four different devices here, two designs, two materials.

The essence of the discussion is that transitional zone, as you described earlier, between the center and the periphery, when you

feel that you have enough evidence to make a decision regarding the Quadra RG and the CRT designs, you are really making a cut on how comfortable you feel with your understanding of this technology at this point to make that adjustment.

I hope that clarified it a little bit.

DR. WEISS: Sponsor, closing comments.

Sponsor - Closing Comments

DR. MEYERS: None.

DR. WEISS: No closing comments by the sponsor.

DR. MEYERS: Thank you very much.

DR. WEISS: Thank you, sir.

We will have the voting options read by Sally Thornton.

Voting Options Read

MS. THORNTON: These are the panel recommendation options for premarket approval applications.

The Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act, as amended by the Safety Medical Devices Act of 1990, allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on

designated medical device premarket approval applications, or PMAs, that are filed with the agency.

The PMA must stand on its own merits and your recommendation must be supported by safety and effectiveness data in the application or by applicable publicly available information.

Safety is defined in the Act as "Reasonable assurance based on valid scientific evidence that the probable benefits to health under conditions on intended use outweigh any probable risks."

Effectiveness is defined as "Reasonable assurance that in a significant portion of the population, the use of the device for its intended uses and conditions of use when labeled will provide clinically significant results."

Your recommendation options for the vote are as follows: You may recommend approval if there are no conditions attached. You may recommend approvable with conditions. The panel may recommend that the PMA be found approvable subject to specified conditions, such as physician or patient education, labeling changes, or a further analysis of existing data.

Prior to voting, all of the conditions should be discussed by the panel.

You may recommend not approvable. The panel may recommend that the PMA is not approvable if the data do not provide a reasonable assurance that the device is safe or if a reasonable assurance has not been given that the device is effective under the conditions of use recommended or suggested in the proposed labeling.

Following the voting, the Chair will ask each panel member to present a brief statement outlining the reasons for their vote.

Thank you.

Panel Recommendations Taken by Vote

DR. WEISS: I will ask for a motion to be made from the floor concerning this PMA.

DR. HARRIS: May I make a recommendation and a suggestion for the panel to vote separately on the CRT design and on the Quadra design? Is that appropriate, Madam Executive Secretary?

MS. THORNTON: I think you have to vote on the PMA and state your conditions or your changes in indications for use or however you want to do it.

DR. WEISS: The motion, you can still

present a motion if you would like, Dr. Harris. Do you have a motion?

DR. HARRIS: I will let somebody else present a motion.

DR. WEISS: Does anyone have a motion to be made from the floor? Dr. Bradley.

DR. BRADLEY: I recommend that we approve with conditions.

DR. McMAHON: Second.

DR. WEISS: Second.

MS. THORNTON: Dr. Saviola has just informed me that the PMA has two separate indications, so you can vote on those two separate indications.

DR. WEISS: Unfortunately, we just had a motion which was seconded.

Do you want to withdraw your motion?

DR. BRADLEY: I would be happy to if somebody would like me to.

DR. WEISS: I am totally unbiased.

DR. ROSENTHAL: I think under the circumstances, since we have been given new information, Dr. Bradley feels you would like to vote separately, he should withdraw his motion.

DR. BRADLEY: I will.